Post Implementation Data Collection & Monitoring

Public Health Assessment of Genetic Tests for Screening & Prevention

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Public health assessment of genetic testing

Evidence-based evaluation needed at two key points:

- Transition from research to clinical practice
- Post-implementation period
  - Demonstrate acceptable performance in practice
  - Assess implementation success and public health impact

Data collection and monitoring in the post-implementation period

- Confirm or update performance estimates
- Assess public health impact – including quality, acceptability, utilization, and access
- Document implementation issues
- Assess fit with healthcare delivery systems
- Resolve gaps in knowledge

Monitoring genetic testing

- We know very little about genetic testing in the United States
- Minimal assessment of genetic testing in clinical or public health practice setting
  - Who is being tested?
  - Who is ordering testing?
  - Why?
  - Where is testing being done?
  - What methods / technologies are used?

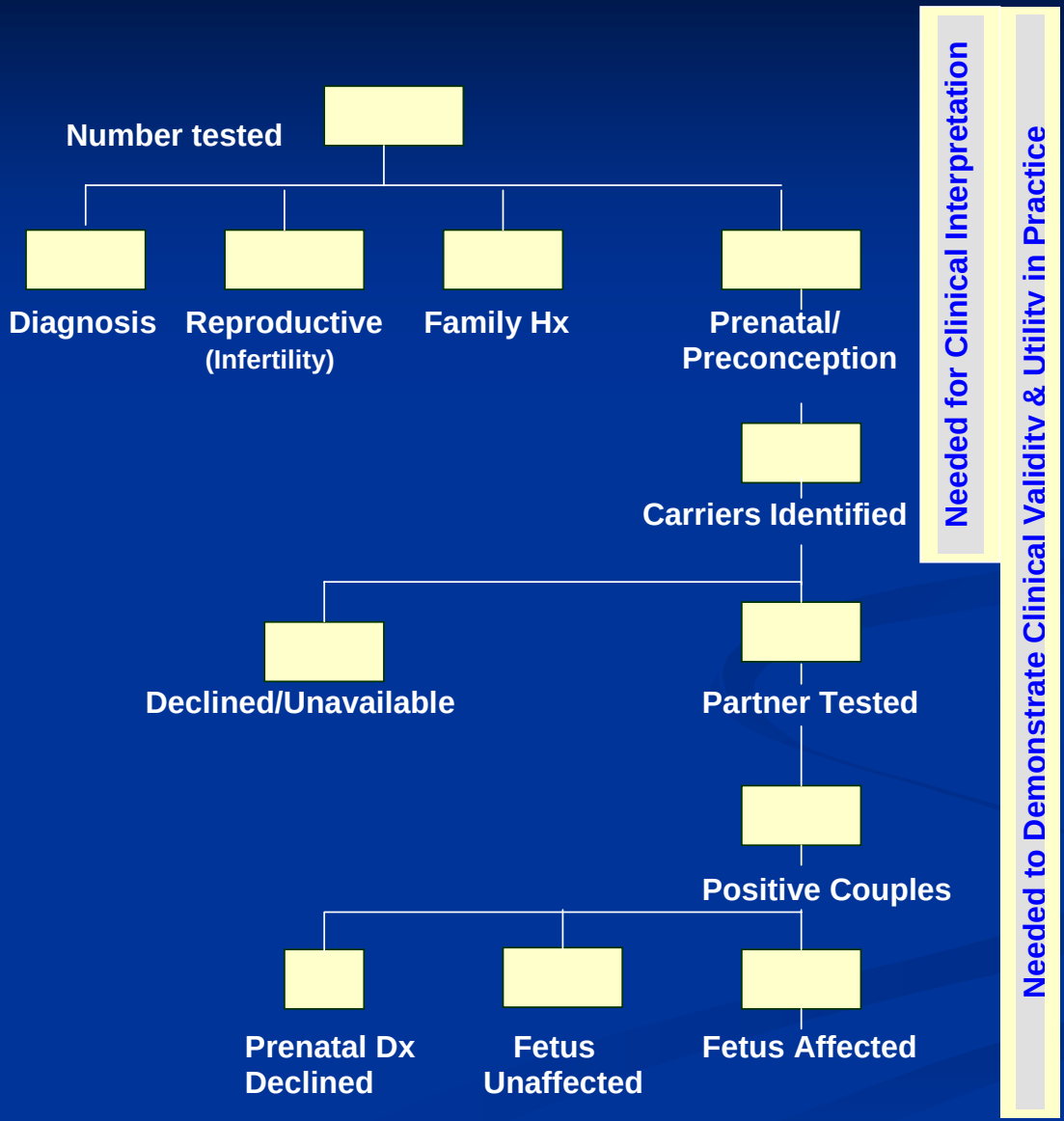
Long-term monitoring can answer questions like:

- Are providers & patients properly educated? Satisfied with the process?
- Is the quality of laboratory service adequate?
  - Are labs able to obtain needed information?
  - Is the panel of mutations appropriate?
  - Is the test being offered appropriately?
  - How are laboratory test results being reported?
- Are performance expectations and pilot trial results being confirmed?
- Are there problems with implementation?

Long-term monitoring can answer questions like:

- What actions are being taken? Are they appropriate?
- Is there a discernable impact on outcomes?
- Are there issues with reimbursement? Access?
- Are safeguards in place to deal with ethical, legal and social issues?
  - Have additional ELSI been identified?
- Are program costs acceptable?
- Should the process or guidelines be modified? Discontinued?

Prenatal CF screening via carrier testing



Collecting Long-term Monitoring Information: Experience of Three CFTR Laboratories

Data Collected	Strom et al, 2001	Clinigene	FBR
All *CFTR* Tests	20,103	3,324	4,260
Screening Tests	Unk	3,298	4,260
Carriers Identified	Unk	132	153
Carrier Rate (uncorr)	Unk	1 in 25	1 in 28
Partners Tested	Unk	55*	153
Positive Couples	Unk	3*	7
Prenatal Diagnosis	Unk	Unk	6
Fetus Affected	Unk	Unk	3

* Known to be under-ascertained

Cystic fibrosis carrier testing

- ACOG/ACMG did not address evaluation
- No group charged with coordinating data collection
  - Laboratories → expense, time, increasing difficulty & no CLIA requirement
  - Providers/payers lack access through claims data
- Anecdotal reports on implementation issues
  - Access to & understanding of guidelines
  - Problems with patient information & result reporting
  - Small number of labs routinely reported 5T
  - Difficult to quantify problems
- Addressing performance in practice
  - Proficiency testing
  - Reports on mutation frequencies

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ACMG Carrier Screening Work Group

- 2001 recommended panel of mutations & variants

  Grody WW et al. Laboratory standards and guidelines for population-based cystic fibrosis carrier screening.

  - Mutation should be present in at least 0.1% of CF patient chromosomes
- 2002 review initiated
  - Information collected by laboratories
    - > 400,000 individuals tested
  - CF Foundation patient mutation database
    - 42,737 CF patient chromosomes
  - Reports of provider experience

ACMG Work Group Questions

Has the observed frequency of any CF mutations changed significantly since 1999?

- Any mutation with prevalence <0.1% should be removed from screening panel → 1078delT removed
- Future decisions based on benefits & costs of incremental gain in performance
  - 6 mutations at frequencies 0.1-0.17% → + 0.77%
  - Weigh against potential increase in error rate & adaptability of current methods / platforms → No additions at this time
  - Local demographics may suggest need to add ethnic-specific mutations

Watson MS et al. Cystic Fibrosis (CF) Couple Carrier Screening: 2004 Revision of ACMG's Mutation Panel. *Genetics in Medicine*, in press.

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ACMG Work Group Questions

Is the prevalence of CF mutations in the general population the same as predicted from the frequency in CF patients?

- I148T occurs 50-100x more frequently in the general population (0.05%)
  - *CFTR* genes in CF patients also have 3199del6 (<0.1%)
  - Vast majority with I148T do not have 3199del6 → I148T removed

Watson MS et al. Cystic Fibrosis (CF) Couple Carrier Screening: 2004 Revision of ACMG's Mutation Panel. *Genetics in Medicine*, in press.

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ACMG Work Group Questions

Evidence of consistent & recurring challenges with interpretation of some mutations in the panel?

- Complexity of association between R117H & 5T variant
- Frequency of R117H-5T appreciable → Retain R117H & use 5T as reflex only when R117H is present
  - Needs educational effort to ensure proper implementation

Watson MS et al. Cystic Fibrosis (CF) Couple Carrier Screening: 2004 Revision of ACMG's Mutation Panel. *Genetics in Medicine*, in press.

Reliability of CF Laboratory Reports

- European Quality Assessment Scheme
  - Routinely collects laboratory reports as part of external proficiency testing
  - Found that 31% of CF reports had errors
- Suggests that it might be important to monitor CF reporting in the US
  - Tulane University/CDC
    - Assess the variability of reports for CF and factor V Leiden testing
    - Assess the usefulness various report formats in interpreting genetic test results

BRCA1/2 testing for susceptibility to breast and ovarian cancer

- What are expected performance characteristics?
- Who is being tested?
  - Geography, demographics, personal/family history
  - Comparison with guidelines
  - Observed mutation rates
- Who orders tests?
  - Geography, demographics, specialty
- Who pays for tests?

- Routine testing since 1996
- Coordination not the issue
  - Technology and data proprietary
- Motivation for service provider?
- Other sources of data?

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So, how do we do it?

- Think programmatically
  - Patient-provider & provider-lab communication
  - Sampling & testing
  - Reporting & result communication ± genetic counseling
  - Facilitating & documenting appropriate follow-up
- Develop plans & partnerships
  - Who is responsible for collecting / evaluating data?
  - What are the key pieces of information to be collected? Measurements / quality indicators to be evaluated?
  - How will the evaluation be funded?
  - What are pre-established expectations / goals that results will be compared to?

Possiblities

- Public-private partnerships / data collaborations
  - Laboratories
  - Providers & health plans
  - Purchasers & payers
  - Organizations / networks
- Utilization surveys
  - Proficiency testing
  - Regulatory – CAP, CMS, states
  - Voluntary
- Surveillance mechanisms
  - Disease registries (CF Foundation)
  - Cancer registries

Long term goals

- Standardization of data collection formats
- Identification of effective quality indicators
- Coordination of care
- Development & funding of research agenda
- Support review of current programs / guidelines / recommendations based on new information
- Create an expectation among providers, payers, policy makers that a certain level of review will occur

Evaluation of Genomic Applications in Practice and Prevention (EGAPP): A Three-Year Model Project

- Utilize
  - historical recommendations for action
  - knowledge gained from ACCE project & other CDC initiatives
  - existing processes for evaluation and appraisal
  - international health technology assessment experience
- Establish & evaluate a systematic & sustainable mechanism for pre- & post-market evaluation of genomic applications in the US

Elements of effective evaluation

- Systematic review & integration of data on analytic and clinical validity
- Unbiased assessment of clinical utility in comparison with outcomes obtained in the absence of testing or using alternative tests
- Identification of ELSI
- Appropriate dissemination of evidence summaries, guidelines, & recommendations to target audiences
- Post-implementation data collection and updating of the knowledge base

EGAPP Working Group

Independent
Non-Federal
Multidisciplinary

- 10-12 experts
  - Health care
  - Public health
  - HuGE
  - Health technology assessment
- In-person meetings

Support & coordination provided by

RTI International / CDC

Roles of Working Group

- Define analytic framework for EBR
  - Transparent process - provide clear linkage between evidence and recommendations
- Engage stakeholders
- Develop criteria, select and prioritize topics
- Request EBR → RTI
- Develop recommendations based on evidence
- Consider strategies for post-implementation monitoring & data collection → RTI
- Address QA & technical issues that arise with general implementation → Appropriate groups
- Take part in evaluation → RTI / CDC

	USPSTF	ACCE Model
Goals	Assess merit of preventive measures (screening tests) Identify research agenda	Evaluate genetic tests before transition into clinical practice Identify gaps in knowledge
Methodology	Analytic framework with key questions that link preventions with outcomes Outcome tables on benefits and harms Focus on clinical utility	44+ targeted questions on ACCE elements plus disorder/ setting Collect, analyze, summarize data using tables & graphics Broader focus – "first look" at all elements
Grading Quality of Evidence	Structured approach for inclusion/exclusion	Ad hoc approach for extracting maximum information
Product	Specific recommendations about use in primary care	Review & interpret data without suggesting policy

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Stakeholders

Health care providers

Consumers

Professional organizations

Policy makers

Public health

Industry / biotechnology

Health care payers & purchasers

Laboratories

Regulatory groups

- Identify & engage
- Needs assessment
  - Specific topics for immediate consideration by WG
  - Content and format of information needed and useful from their perspectives
- Content experts
- Involvement in developing informational messages for key target audiences

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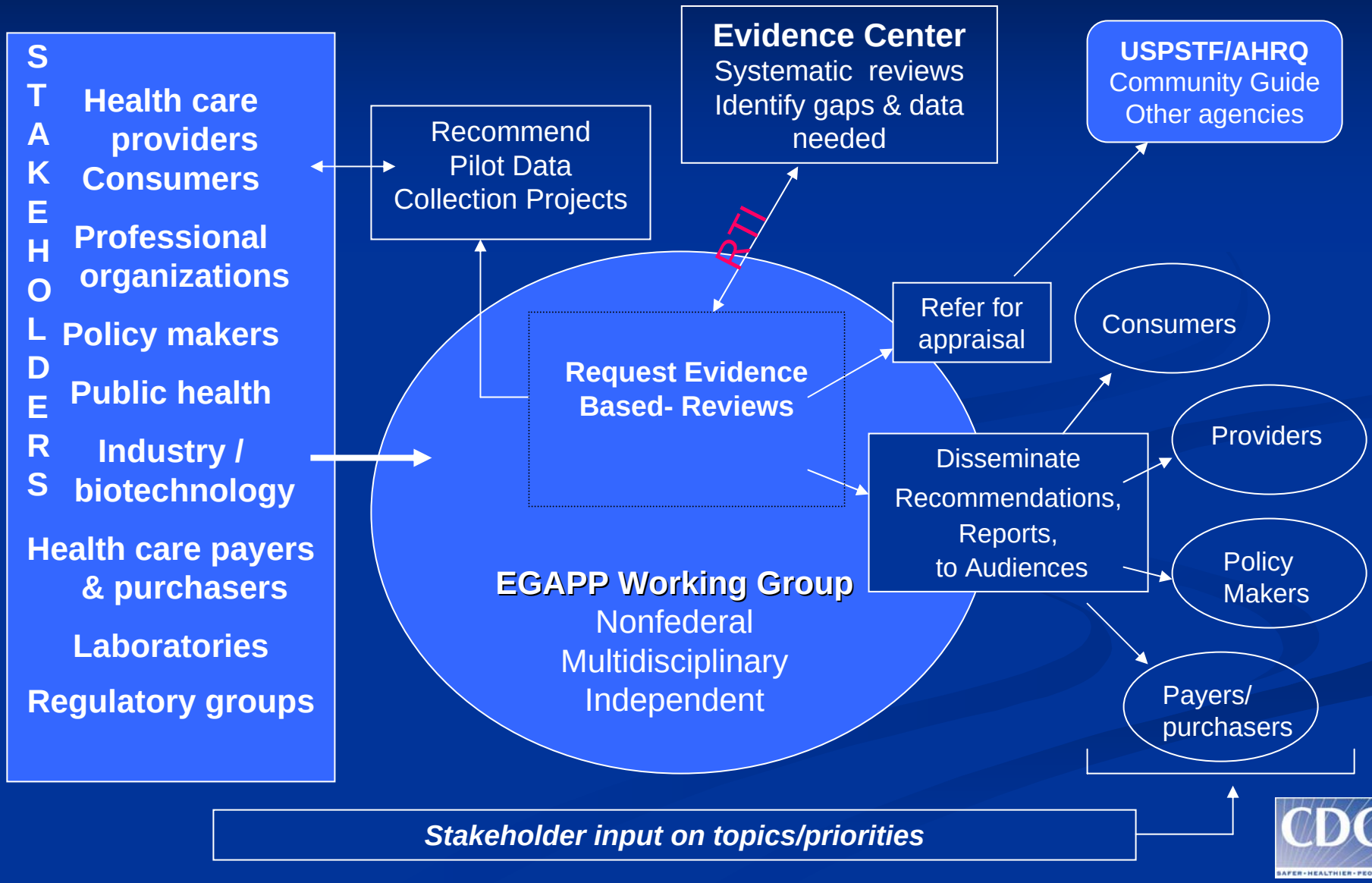
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Health care providers
Consumers
Professional organizations
Policy makers
Public health
Industry / biotechnology
Health care payers & purchasers
Laboratories
Regulatory groups
Recommend Pilot Data Collection Projects
Evidence Center
Systematic reviews
Identify gaps & data needed
USPSTF/AHRQ
Community Guide
Other agencies
RTI
Request Evidence Based- Reviews
Refer for appraisal
Consumers
Disseminate Recommendations, Reports, to Audiences
Providers
Policy Makers
Payers/ purchasers
EGAPP Working Group
Nonfederal
Multidisciplinary
Independent
Stakeholder input on topics/priorities

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